

SEQUENCE LISTING

<110> ROZEN, Rima

<120> cDNA FOR HUMAN METHYLENETETRAHYDROFOLATE  
REDUCTASE AND USES THEREOF

<130> 04844/005005

<150> US 09/592,595  
<151> 2000-06-12

<150> US 09/258,928  
<151> 1999-03-01

<150> US 08/738,000  
<151> 1997-02-12

<150> PCT/CA95/00314  
<151> 1995-05-25

<150> GB 9410620.0  
<151> 1994-05-26

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ccc tgc ttg gag ggc agt gcc agc agt ggc agt gag agc tcc aaa gat		96
Pro Cys Leu Glu Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp		
20 25 30		
agt tcg aga tgt tcc acc ccg ggc ctg gac cct gag cgg cat gag aga		144
Ser Ser Arg Cys Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg		
35 40 45		
ctc cgg gag aag atg agg cgg cga ttg gaa tct ggt gac aag tgg ttc		192
Leu Arg Glu Lys Met Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe		
50 55 60		
tcc ctg gaa ttc ttc cct cct cga act gct gag gga gct gtc aat ctc		240
Ser Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu		

65	70	75	80	
atc tca agg ttt gac	cgg atg gca gca	ggt ggc ccc ctc	tac ata gac	288
Ile Ser Arg Phe Asp	Arg Met Ala Ala	Gly Gly Pro Leu	Tyr Ile Asp	
85	90	95		
gtg acc tgg cac cca	gca ggt gac cct	ggc tca gac aag	gag acc tcc	336
Val Thr Trp His Pro	Ala Gly Asp Pro	Gly Ser Asp Lys	Glu Thr Ser	
100	105	110		
tcc atg atg atc gcc	agc acc gcc gtg	aac tac tgt ggc	ctg gag acc	384
Ser Met Met Ile Ala	Ser Thr Ala Val	Asn Tyr Cys Gly	Leu Glu Thr	
115	120	125		
atc ctg cac atg acc	tgc cgt cag cgc	ctg gag gag	atc acg ggc	432
Ile Leu His Met Thr	Cys Cys Arg Gln	Arg Leu Glu	Glu Ile Thr Gly	
130	135	140		
cat ctg cac aaa gct	aag cag ctg ggc	ctg aag aac atc	atg gcg ctg	480
His Leu His Lys Ala	Lys Gln Leu Gly	Leu Lys Asn	Ile Met Ala Leu	
145	150	155	160	
cg gga gac cca ata	ggt gac cag tgg	gaa gag gag gag	gga ggc ttc	528
Arg Gly Asp Pro Ile	Gly Asp Gln Trp	Glu Glu Glu Gly	Gly Phe	
165	170	175		
aac tac gca gtg gac	ctg gtg aag cac	atc cga agt gag	ttt ggt gac	576
Asn Tyr Ala Val Asp	Leu Val Lys His	Ile Arg Ser Glu	Phe Gly Asp	
180	185	190		
tac ttt gac atc tgt	gtg gca ggt tac	ccc aaa ggc cac	ccc gaa gca	624
Tyr Phe Asp Ile Cys	Val Ala Gly Tyr	Pro Lys Gly	His Pro Glu Ala	
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Gly Ser Phe Glu Ala	Asp Leu Lys His	Leu Lys Glu Lys	Val Ser Ala	
210	215	220		
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Gly Ala Asp Phe Ile	Ile Thr Gln Leu	Phe Glu Ala Asp	Thr Phe	
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ttc cgc ttt gtg aag	gca tgc acc gac	atg ggc atc act	tgc ccc atc	768
Phe Arg Phe Val Lys	Ala Cys Thr Asp	Met Gly Ile Thr	Cys Pro Ile	
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Val Pro Gly Ile Phe	Pro Ile Gln Gly	Tyr His Ser Leu	Arg Gln Leu	
260	265	270		
gtg aag ctg tcc aag	ctg gag gtg cca	cag gag atc aag	gac gtg att	864
Val Lys Leu Ser Lys	Leu Glu Val Pro	Gln Glu Ile Lys	Asp Val Ile	
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gag cca atc aaa gac	aac gat gct gcc	atc cgc aac tat	ggc atc gag	912
Glu Pro Ile Lys Asp	Asn Asp Ala Ala	Ile Arg Asn Tyr	Gly Ile Glu	
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Gly Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val			
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Leu Lys Arg Leu Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro			
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Trp Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro			
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Ile Phe Trp Ala Ser Arg Pro Lys Ser Tyr Ile Tyr Arg Thr Gln Glu			
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Trp Asp Glu Phe Pro Asn Gly Arg Trp Gly Asn Ser Ser Ser Pro Ala			
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Phe Gly Glu Leu Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser			
405	410	415	
ccc aag gag gag ctg ctg aag atg tgg ggg gag gag ctg acc agt gaa			1296
Pro Lys Glu Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu			
420	425	430	
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Ala Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn			
435	440	445	
cgg aat ggt cac aaa gtg act tgc ctg ccc tgg aac gat gag ccc ctg			1392
Arg Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu			
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gcg gct gag acc agc ctg ctg aag gag gag ctg ctg cgg gtg aac cgc			1440
Ala Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg			
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cag ggc atc ctc acc atc aac tca cag ccc aac atc aac ggg aag ccg			1488
Gln Gly Ile Leu Thr Ile Asn Ser Gln Pro Asn Ile Asn Gly Lys Pro			
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Ser Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe			
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Gln Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala			
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ctt ctg caa gtg ctg aag aag tac gag ctc cgg gtt aat tac cac ctt			1632
Leu Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu			
530	535	540	

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acc gta gtg gat ccc gtc agc ttc atg ttc tgg aag gac gag gcc ttt Thr Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe 580 585 590	1776
gcc ctg tgg att gag cgg tgg gga aag ctg tat gag gag gag tcc ccg Ala Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Ser Pro 595 600 605	1824
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acg gag gct cca tgaccctgcg tcctgacgcc ctgcgttga gccactcctg Thr Glu Ala Pro 660	2020
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Leu Arg Glu Lys Met Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe 50 55 60	
Ser Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu 65 70 75 80	
Ile Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp 85 90 95	
Val Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser 100 105 110	
Ser Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr 115 120 125	

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 His Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu  
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 Glu Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu  
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 Gly Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val  
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 Trp Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro  
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 385 390 395 400  
 Phe Gly Glu Leu Lys Asp Tyr Tyr Leu Phe Tyr Leu Lys Ser Lys Ser  
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 Pro Lys Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu  
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 Ala Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn  
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 Ser Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe  
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 Gln Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala  
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 Leu Leu Gln Val Leu Lys Lys Tyr Glu Leu Arg Val Asn Tyr His Leu  
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 Val Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro  
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 Asn Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro  
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 Thr Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe  
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 Ala Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Ser Pro

595	600	605
Ser Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn		
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   Cys Leu Glu Gly Ser Ala Ser Ser Gly Ser Glu Ser Ser Lys Asp Ser  
   15                         20                         25  
  
 tcg aga tgt tcc acc ccg ggc ctg gac cct gag cgg cat gag aga ctc  
   Ser Arg Cys Ser Thr Pro Gly Leu Asp Pro Glu Arg His Glu Arg Leu  
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 cg<sup>g</sup> gag aag atg agg cg<sup>g</sup> cga ttg gaa tct ggt gac aag tgg ttc tcc  
   Arg Glu Lys Met Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser  
   50                         55                         60  
  
 ctg gaa ttc ttc cct cct cga act gct gag gga gct gtc aat ctc atc  
   Leu Glu Phe Phe Pro Pro Arg Thr Ala Glu Gly Ala Val Asn Leu Ile  
   65                         70                         75  
  
 tca agg ttt gac cg<sup>g</sup> atg gca gca ggt ggc ccc ctc tac ata gac gtg  
   Ser Arg Phe Asp Arg Met Ala Ala Gly Gly Pro Leu Tyr Ile Asp Val  
   80                         85                         90  
  
 acc tgg cac cca gca ggt gac cct ggc tca gac aag gag acc tcc tcc  
   Thr Trp His Pro Ala Gly Asp Pro Gly Ser Asp Lys Glu Thr Ser Ser  
   95                         100                         105  
  
 atg atg atc gcc agc acc gcc gtg aac tac tgt ggc ctg gag acc atc  
   Met Met Ile Ala Ser Thr Ala Val Asn Tyr Cys Gly Leu Glu Thr Ile  
   110                         115                         120                         125  
  
 ctg cac atg acc tgc tgc cgt cag cgc ctg gag gag atc acg ggc cat  
   Leu His Met Thr Cys Cys Arg Gln Arg Leu Glu Glu Ile Thr Gly His  
   130                         135                         140  
  
 ctg cac aaa gct aag cag ctg ggc ctg aag aac atc atg gcg ctg cgg  
   Leu His Lys Ala Lys Gln Leu Gly Leu Lys Asn Ile Met Ala Leu Arg

145

150

155

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Gly Asp Pro Ile Gly Asp Gln Trp Glu Glu Glu Glu Gly Gly Phe Asn	
160 165 170	
tac gca gtg gac ctg gtg aag cac atc cga agt gag ttt ggt gac tac	579
Tyr Ala Val Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr	
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Phe Asp Ile Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly	
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Ala Asp Phe Ile Ile Thr Gln Leu Phe Phe Glu Ala Asp Thr Phe Phe	
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Arg Phe Val Lys Ala Cys Thr Asp Met Gly Ile Thr Cys Pro Ile Val	
240 245 250	
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Pro Gly Ile Phe Pro Ile Gln Gly Tyr His Ser Leu Arg Gln Leu Val	
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aag ctg tcc aag ctg gag gtg cca cag gag atc aag gac gtg att gag	867
Lys Leu Ser Lys Leu Glu Val Pro Gln Glu Ile Lys Asp Val Ile Glu	
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Pro Ile Lys Asp Asn Asp Ala Ala Ile Arg Asn Tyr Gly Ile Glu Leu	
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Leu His Phe Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val Leu	
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Lys Arg Leu Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro Trp	
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Ala Leu Ser Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro Ile	
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Phe Trp Ala Ser Arg Pro Lys Ser Tyr Ile Tyr Arg Thr Gln Glu Trp	
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Asp Glu Phe Pro Asn Gly Arg Trp Gly Asn Ser Ser Ser Pro Ala Phe			
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Lys Glu Glu Leu Leu Lys Met Trp Gly Glu Glu Leu Thr Ser Glu Ala			
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Ser Val Phe Glu Val Phe Val Leu Tyr Leu Ser Gly Glu Pro Asn Arg			
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aat ggt cac aaa gtg act tgc ctg ccc tgg aac gat gag ccc ctg gcg			1395
Asn Gly His Lys Val Thr Cys Leu Pro Trp Asn Asp Glu Pro Leu Ala			
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Ala Glu Thr Ser Leu Leu Lys Glu Glu Leu Leu Arg Val Asn Arg Gln			
465	470	475	
ggc atc ctc acc atc aac tca cag ccc aac atc aac ggg aag ccg tcc			1491
Gly Ile Leu Thr Ile Asn Ser Gln Pro Asn Ile Asn Gly Lys Pro Ser			
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Ser Asp Pro Ile Val Gly Trp Gly Pro Ser Gly Gly Tyr Val Phe Gln			
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Lys Ala Tyr Leu Glu Phe Phe Thr Ser Arg Glu Thr Ala Glu Ala Leu			
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Leu Gln Val Leu Lys Tyr Glu Leu Arg Val Asn Tyr His Leu Val			
530	535	540	
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Asn Val Lys Gly Glu Asn Ile Thr Asn Ala Pro Glu Leu Gln Pro Asn			
545	550	555	
gct gtc act tgg ggc atc ttc cct ggg cga gag atc atc cag ccc acc			1731
Ala Val Thr Trp Gly Ile Phe Pro Gly Arg Glu Ile Ile Gln Pro Thr			
560	565	570	
gta gtg gat ccc gtc agc ttc atg ttc tgg aag gac gag gcc ttt gcc			1779
Val Val Asp Pro Val Ser Phe Met Phe Trp Lys Asp Glu Ala Phe Ala			
575	580	585	
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Leu Trp Ile Glu Arg Trp Gly Lys Leu Tyr Glu Glu Glu Ser Pro Ser			
590	595	600	605
cgc acc atc atc cag tac atc cac gac aac tac ttc ctg gtc aac ctg			1875
Arg Thr Ile Ile Gln Tyr Ile His Asp Asn Tyr Phe Leu Val Asn Leu			
610	615	620	

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Val Asp Asn Asp Phe Pro Leu Asp Asn Cys Leu Trp Gln Val Val Glu	
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635	
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Met Arg Arg Arg Leu Glu Ser Gly Asp Lys Trp Phe Ser Leu Glu Phe	
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Asp Leu Val Lys His Ile Arg Ser Glu Phe Gly Asp Tyr Phe Asp Ile	
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Cys Val Ala Gly Tyr Pro Lys Gly His Pro Glu Ala Gly Ser Phe Glu	
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 305 310 315 320  
 Tyr Thr Leu Asn Arg Glu Met Ala Thr Thr Glu Val Leu Lys Arg Leu  
 325 330 335  
 Gly Met Trp Thr Glu Asp Pro Arg Arg Pro Leu Pro Trp Ala Leu Ser  
 340 345 350  
 Ala His Pro Lys Arg Arg Glu Glu Asp Val Arg Pro Ile Phe Trp Ala  
 355 360 365  
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